

Comment Number	Guideline Document Paragraph (§)	Comments
1	20	AVMA 2007 reference does not match the citation in REFERENCES section (i.e., AVMA 2001). The 2000 Report on the AVMA Panel on Euthanasia has been superseded by the AVMA Guidelines on Euthanasia (June 2007). For the most current version of the Guidelines, see: http://www.avma.org/issues/animal_welfare/euthanasia.pdf
2	23	<i>...fixation should continue for no less than 24-48 hours prior to trimming...</i> TGs 412 and 413 do not provide a range; state <i>...no less than 48 hours...</i> ; consider harmonizing this with the TGs.
3	23; Table 3	The list of organs and tissues that should be preserved during necropsy is similar to the table in TG 413 but more detailed than the table in TG 412; consider harmonizing this table and those in the test guidelines; highlight the organs that should be weighed wet (e.g., boldface as in TGs 412 and 413).
4	36	The guidance document should cite the references that provided the information associated with the referenced internet site (http://reni.item.fraunhofer.de/reni/trimming/index.php): Ruehl-Fehlert C, Kittel B, Morawietz G, Deslex P, Keenan C, Mahrt CR, Nolte T, Robinson M, Stuart BP, Deschl U (2003) Revised guides for organ sampling and trimming in rats and mice - Part 1. Exp Toxicol Pathol 55: 91–106. Kittel B, Ruehl-Fehlert C, Morawietz G, Klapwijk J, Elwell MR, Lenz B, O'Sullivan MG, Roth DR, Wadsworth PF (2004) Revised guides for organ sampling and trimming in rats and mice - Part 2. Exp Toxicol Pathol 55: 413–431. Morawietz G, Ruehl-Fehlert C, Kittel B, Bube A, Keane K, Halm S, Heuser A, Hellmann J (2004) Revised guides for organ sampling and trimming in rats and mice - Part 3. Exp Toxicol Pathol 55: 433–449.
5	46	Reference to histopathological evaluation of all organs and tissues listed in Table 3 (see above) should be harmonized with TGs 412 and 413.

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6	47	<p>Provide suggested references for standard veterinary pathology nomenclature; provide note about sponsors of the goRENI nomenclature and diagnostic criteria website (http://www.goreni.org) (e.g., European Society of Toxicologic Pathology, British Society of Toxicological Pathologists)</p>
7	70	<p>Because both TGs (412 and 413) have more than a single treated group, and because TG413 gives the investigator the discretion to include satellite and/or interim-sacrifice groups, it is important that the text on statistics identify that these, too, are reasons to be sure to consult a professional statistician. Suggest the text be amended as follows:</p> <p>“... Choosing appropriate statistical tests may require assistance from a professional biostatistician. Fisher's Exact and Kolmogorov-Smirnov tests have proven to be appropriate and useful for evaluating and interpreting the incidence and severity of respiratory tract lesions. <i>Because there are multiple exposed groups, and there may be satellite or interim-sacrifice groups, analyses will benefit from holistic or all-inclusive statistical consideration, with attention paid to the possible presence of trend.</i> In evaluating statistical data it is important to keep in mind the normal range of biological variation, utilize concurrent as well as historical control data, and consider findings that, although not statistically significant, may suggest an effect of exposure to the test material.”</p> <p>Delete reference to Fisher's Exact Test because its proper use would require adjustment of the test level for multiple comparisons and such detail is not being provided.</p>